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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/664,127	09/18/2000	Wolfgang H. Dillmann	220002057202	9042

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EXAMINER

CHEN, SHIN LIN

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 05/02/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/664,127

Applicant(s)
Dillmann et al.

Examiner
Shin-Lin Chen

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1632



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Feb 19, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above, claim(s) 10-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 21-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 12 6) ☐ Other:

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DETAILED ACTION

Applicants' amendment and supplemental information disclosure statement filed 2-19-03 have been entered. Claims 1, 7 and 25 have been amended. Claims 33-40 have been added. Claims 1-40 are pending and claims 1-9 and 21-40 are under consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-4 and 26-32 remain rejected and claims 33-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mestril et al., 1994 (J. Clin. Invest., Vol. 93, p. 759-767) in view of Giordano et al., 1993 (Circulation, Vol. 88, p. I-139) and Hayden et al., 1997 (US

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Patent No. 5,658,729) and is repeated for the reasons set forth in the preceding Official action mailed 10-17-02 (Paper No. 10). Applicant's arguments filed 2-19-03 have been fully considered but they are not persuasive.

The newly added claims 33-40 specify the vector of claim 1 or 5 to HSP70i, HSP27, HSP40 or HSP60.

Applicants argue that Mestril does not teach or suggest a replication-deficient recombinant adenoviral vector or the use of CMV or myocyte-specific promoter, Giordano does not teach replication-deficient recombinant adenoviral vector comprising a heat shock protein and method of producing said replication-deficient adenoviral vector or composition comprising such vector, and Giordano suggests methods for transfection without constructing recombinant AdV. Applicants further argue that Hayden does not teach or suggest a recombinant, replication-deficient adenoviral vector expressing heat shock protein, host cells or composition comprising said vector, or methods of making said vector (amendment, p. 5, 6).

This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-17-02 (Paper No. 10). The rejection under 35 U.S.C. 103(a) does not require every cited reference to teach every element of the claimed invention. Mestril teaches "Myocardial ischemia markedly increases the expression of several members of the stress/heat shock protein (HSP) family, especially the inducible HSP70 isoforms" and constructs a plasmid vector pSVTK-human HSP70 expressing human HSP70 under the control of TK promoter and the SV40 enhancer, and transfect rat embryonic heart-derived myogenic cell line H9c2(2-1) with

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said vector. Although Mestril does not teach or suggest a replication-deficient recombinant adenoviral vector or the use of CMV or myocyte-specific promoter, Giordano does teach that recombinant replication deficient adenoviral vector is an effective vector for delivery of foreign or endogenous genes to myocardium and endothelium. Both Plasmid and adenoviral vector are DNA vectors and Giordano teaches high transfection efficiency (greater than 80%) in cultured adult rat cardiomyocytes using recombinant AdV expressing LacZ, thus, the teaching of Giordano would have motivated one of ordinary skill in the art at the time of the invention to use a recombinant replication deficient adenoviral vector expressing a heat shock protein for gene delivery to cells *in vitro* or *in vivo*. Although Giordano suggests a method for high efficiency transfection in adult cardiomyocyte without the need for constructing recombinant AdV, this method is just an alternative of a recombinant replication deficient adenovirus (AdV) for gene transfer. Giordano's suggestion does not preclude one of ordinary skill from using an AdV for gene delivery, in fact, Giordano teaches that AdV is an effective vector for delivery of foreign or endogenous genes to myocardium and endothelium. Further, Hayden teaches preparation of a replication-deficient recombinant adenoviral vector lacking E1 or E3 genes and expressing lipoprotein lipase (LPL), and use of said adenoviral vector in gene therapy for treating LPL deficiencies. Hayden also teaches using RSV promoter or CMV promoter for the expression LPL gene product and suggest using a muscle-specific promoter in place of CMV promoter for the purpose of tissue-specific expression of gene of interest. It was well known in the art to substitute a promoter with another promoter in a vector. It would have been obvious for one of

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ordinary skill to substitute the TK promoter as taught by Mestril with CMV promoter or muscle-specific promoter according to the teachings of Giordano and Hayden. Thus, one of ordinary skill in the art at the time of the invention would have been motivated to construct a recombinant replication-deficient adenoviral vector lacking E1A/E1B genes and expressing a heat shock protein, such as HSP70, under the control of CMV promoter or a myocyte-specific promoter, a host cell comprising said vector, and a composition comprising said vector according to the collective teachings of Mestril, Giordano and Hayden.

Since Mestril teaches “Myocardial ischemia markedly increases the expression of several members of the stress/heat shock protein (HSP) family” and HSP27, HSP40 and HSP60 were known in the art, one ordinary skill in the art at the time of the invention would have been motivated to construct a recombinant replication-deficient adenoviral vector expressing a HSP27, HSP40 or HSP60 to transfect myogenic cells and study the resistance of the transfected cells to an ischemic-like stress as compared to control myogenic cells according to the collective teachings of Mestril, Giordano and Hayden as discussed above.

Applicants argue that there is no suggestion to combine the cited references and the combination of those references is the result of the use of hindsight reconstruction (amendment, p. 6, last paragraph). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of

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ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Thus, Applicants' argument is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-17-02 (Paper No. 10) and the reasons set forth above.

It should be noted that how and where the examination of the present application is to be examined would be the decision of the USPTO and **NOT to be intervened** by applicants or applicants' representative.

3. Claims 1, 5, 7-9, and 21-24 remain rejected and claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mestril et al., 1994 (J. Clin. Invest., Vol. 93, p. 759-767) in view of Giordano et al., 1993 (Circulation, Vol. 88, p. I-139) and Hayden et al., 1997 (US Patent No. 5,658,729) as applied to claims 1-4 and 25-32 above, and further in view of McGrory et al., 1988 (Virology, Vol. 163, p. 614-617) and is repeated for the reasons set forth in the preceding Official action mailed 10-17-02 (Paper No. 10). Applicant's arguments filed 2-19-03 have been fully considered but they are not persuasive.

Claim 25 has been amended to depend on claim 21, therefore, claim 25 that was originally rejected under the first section of 35 U.S.C. 103(a) rejection has been moved to this 35 U.S.C. 103(a) rejection.

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Applicants argue that there is no motivation or suggestion to combine the cited references, Mestril, Giordano and Hayden and McGrory, and reiterate arguments regarding Mestril, Giordano and Hayden. Applicants further argue that McGrory does not teach replication-deficient adenoviral vector expressing a heat shock protein, host cells and compositions comprising or methods of making, and the combination of the references is a hindsight reconstruction (amendment, p. 7, 8). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 10-17-02 (Paper No. 10) and the reasons set forth above.

Conclusion

4. Claims 1-5, 7-9 and 21-32 remain rejected and claims 33-40 are rejected. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

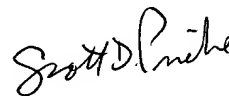
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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.


SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER

Shin-Lin Chen, Ph.D.